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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,264	12/03/2001	Laurie H. Glimcher	HUI-040CP	2529

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EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/008,264	GLIMCHER ET AL.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,8-12,50,51,53-55,57,58,61-75,78-84 and 87-112* is/are pending in the application.

4a) Of the above claim(s) *87-112* is/are withdrawn from consideration.

5)☒ Claim(s) *1,2 and 8-12* is/are allowed.

6)☒ Claim(s) *4, 6, 50-51, 53-55, 57-58, 61-75, and 78-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 6/30/06, are acknowledged.

Claims 1-2, 4, 6, 50-51, 53, 55, 57-58, 84, 87-95, 98, 100-102 and 102 have been amended.
Claims 76-77, 85-86, and 113-114 have been cancelled.
Claims 1-2, 4, 6, 8-12, 50-51, 53-55, 57-58, 61-75, 78-84, 87-112 are pending.

Claims 87-112 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-2, 4, 6, 8-12, 50-51, 53-55, 57-58, 61-75, 78-84 are being acted upon.

2. Applicant's amendment to the specification to recite SEQ ID NOS is sufficient to overcome the objection for lack of sequence compliance under C.F.R. 1.821-1.825.

3. Applicant's amendment to the claims is sufficient to overcome the rejections under 35 U.S.C. 112 second paragraph.

4. Applicants amendment to the claims is sufficient to overcome the rejection under 35 U.S.C. 112 first paragraph as it pertains to lack of written description for "complements".

5. The rejection under 112 first paragraph for new matter, as outlined in section A) of the previous office action is withdrawn, in view of Applicant's disclosure on pg. 19 of the specification.

6. The rejection of the claims under 35 U.S.C. 102 is withdrawn in view of Applicant's amendment to recite that the complement is complementary over its full length.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 57 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

B) The variously claimed nucleic acid molecules "labeled with a detectable substance" (Claim 57 and 85-86).

In the Preliminary Amendment filed 10/25/04, Applicant indicates that support for the limitations of Claims 54 can be found at page 24 of the specification, and that support for the limitations of Claims 57 can be found at page 37.

A review of the specification fails to reveal support for the new limitations.

Regarding B), at page 37, the specification discloses labeled nucleic acid probes that hybridize to T-bet mRNA, including probes such as the T-bet DNA of SEQ ID NO: 1 or 3. This specific example of labeled probes comprising SEQ ID NO: 1 or 3 is insufficient to provide adequate support for new claims drawn to a detectably labeled nucleic acid which encodes SEQ ID NO: 2 or a polypeptide 95% identical to SEQ ID NO: 2, or a detectably labeled nucleic acid which has at least 90% identity with SEQ ID NO: 1.

Applicant's arguments, filed 6/30/06, have been fully considered but they are not persuasive.

Applicant argues that the disclosure of labeled nucleic acid probes that hybridize to T-bet mRNA , including SEQ ID NO: 1 and 3, provides adequate support for the limitations of claim 57.

However, it is noted that claim 57, as amended, depends from claim 51, which recites an isolated nucleic acid molecule which hybridizes to the complement of SEQ ID NO: 1 over the full length. Therefore, the disclosure of labeled "probes" does not provide adequate support for the instant claim. Furthermore, the only recited examples of said probes are SEQ ID NO: 1 and 3, and the instant claim is drawn a nucleic acid molecules that hybridizes to the "complement of" SEQ ID NO:1.

9. Claims 4, 6, 50, 53, 64-75, and 78-84 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of nucleic acids that are "90% identical with SEQ ID NO:1", "encodes a polypeptide 95% identical to SEQ ID NO: 2", or "a fragment of at lest 700 contiguous nucleotides of SEQ ID NO: 1".

As set forth previously, nucleic acids that are "90% identical with SEQ ID NO:1" or "encode a polypeptide 95% identical to SEQ ID NO: 2" is the recitation of a broad genus of nucleic acid molecules. For example, SEQ ID NO: 1 is ~1600 nucleotides in length. Therefore, nucleic acids "90% identical" with SEQ ID NO: 1 might be approximately 160 nucleotides (i.e. about 10%) different than SEQ ID NO: 1. Thus, the claims encompass a virtually unlimited number of nucleic acids with mutations, deletions or additions up to ~160 nucleotides in length. Furthermore, the only claimed functional limitation for said nucleic acids is binding to a consensus T-box site. Therefore, the claims encompass nucleic acids that encode proteins that only bind to a T-box site, but might not mediate any other T-bet function (for example the ability to induce IFN-γ production). Thus, these nucleic acids might differ functionally in that some might encode a protein that induces IFN-γ while some might only be able to bind a T-box site. Furthermore, the claims also encompass fragments of SEQ ID NO: 1 "of at least 700 contiguous nucleotides in length". Since SEQ ID NO: 1 is ~1600 nucleotides, the genus encompassed by said fragments is extremely large. In addition, there is no limitation that the fragments of claim 55 even function to encode a functional T-bet protein. Furthermore, Applicant has not disclosed any species of nucleic acids "90% identical", 95% identical" or any specific nucleic acid fragments. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

Applicant's arguments, filed 6/30/06, have been fully considered but they are not persuasive.

Applicant argues that the written description guideline training materials provides an example that proteins having 95% structurally identity and capable of performing a specified function, along with the disclosure of a single species, that meets the written description requirement.

However, it is noted that claim 4 and 6 of the instant application are directed to a nucleic acid molecule that is "90% identical" with SEQ ID NO:1, and therefore do not meet the limitations of the written description guidelines cited by Applicant. Additionally, Claim 4 only requires 90% identity with 700 nucleotides (less than half of SEQ ID NO: 1). With regard to claim 53, while the claim recites an isolated nucleic acid molecule which encodes a polypeptide with "95% identity", the recited function of said polypeptide is that it binds to a

T-box site in DNA and "modulates" IFN-γ production. Therefore, the instant claims encompass a genus of nucleic acid molecules that are capable of "modulating" IFN-γ. For example, the claims might encompass nucleic acid molecules that can increase or decrease IFN-γ (i.e. "modulate"). The claims might even encompass nucleic acids that turn IFN-γ on or off, or those that result in intermittent modulation. In contrast, Applicant has only described nucleic acid molecules that induce IFN-γ production. Therefore, Applicant has not provided adequate written description to demonstrate that they are in possession of the genus of molecules capable of "modulating" IFN-γ.

10. The following are new grounds of rejection necessitated by Applicant's amendment.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6, 50-51, 53, 57, 64-75, 78-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 4, 6, 51, and 53 are indefinite in the recitation of a nucleic acid encoding a polypeptide that "modulates" IFN-γ production. The term "modulates" is a relative term that renders the claims indefinite. It not clear what degree, direction, or type of modulation is required. For example, are the claimed nucleic acids required to encode a protein that induces or suppresses IFN-γ? Additionally, modulate might indicate that IFN-γ is turned on or off, or could also indicate that IFN-γ is upregulated or downregulated to an unspecified degree. In addition, said modulation could be intermittent, or constant.

12. Claims 4, 6, 50-51, 53, 57, 64-75, 78-84 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

Nucleic acids which encode polypeptides that "modulate IFN-γ production (Claims 4, 6, 51, 53, and dependent claims 50, 57, 64-75, and 78-84).

It is noted that applicant has not cited any support for the new limitation in the specification. A review of the specification fails to reveal support for the new limitation.

The instant specification discloses on page 14 that T-bet induces IFN-γ production. It is noted that the term "modulates" encompasses both upregulating and downregulating, and thus has a much broader scope than "induces". The instant specification does not disclose nucleic acid molecules encoding polypeptides that "modulate" IFN-γ, as now claimed

13. Claims 4, 6, 50-51, 53, 57, 64-75, 78-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a polypeptide that has the activity of inducing IFN-γ production in $CD4^+$ cells, does not reasonably provide enablement for:

a polypeptide that "modulates IFN-γ production".

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how

to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The instant claims encompass nucleic acids that encode polypeptides that "modulate" IFN-γ production. It is noted that the term "modulate" encompass both inducing and suppressing IFN-γ production. It is known in the art that T-bet polypeptides (i.e. the polypeptide encoded by SEQ ID NO: 1) induce IFN-γ production from CD4 T cells (see Szabo et al., 2000, of record). Therefore, it seems unlikely that a nucleic acid molecule with 90% identity to T-bet would be capable of also suppressing IFN-γ, as encompassed by the instant claims. Furthermore, the instant specification discloses on pages 75-76 that in contrast to $CD4^+$ cells, T-bet is not involved in controlling IFN-γ production in $CD8^+$ T cells. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with the instant claims, which encompass nucleic acids encoding polypeptides that "modulate" IFN-γ production in any cell.

14. Claims 1-2 and 8-12 are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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August 15, 2006

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